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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,409	03/23/2004	Raymond Pratt	223389	2310

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VENABLE LLP
P.O. BOX 34385
WASHINGTON, DC 20043-9998

EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/806,409	PRATT, RAYMOND	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 11/20/2006, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 21-40 are currently pending and are the subject of this Office Action.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 36 is rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for treating dementia caused by Parkinson's disease, does not reasonably provide enablement for treating one or more motor dysfunctions caused by Parkinson's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.

In re Wright, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) The breadth of the claims.

[1] As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The invention relates to the treatment of one or more "motor dysfunctions" caused by Parkinson's disease by administering donepezil. The relative skill of those in the art is high, generally that of an M.D. or Ph.D. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Mentis *et al.* (Movement Disorders, 2006, vol. 21, pages 549-555) and Fabbrini *et al.* (Acta Neurol. Scand., 2001, vol. 103, pages 123-125) (cited by applicant).

Mentis *et al.*, cited for evidentiary purposes, teaches that anticholinesterase drugs are being prescribed off label for nonmotor symptoms in Parkinson's disease. Theoretically, these drugs can *impair* motor function (Abstract). Subjects were administered donepezil (10 mg/day) and motor function evaluated (pages 549-551). Donepezil had little to no effect on motor function (either positive or negative) in Parkinson patients (pages 552-554).

Fabbrini *et al.*, also cited for evidentiary purposes, teaches that donepezil, a centrally acting cholinesterase inhibitor, was not effective on cognitive dysfunction and did not change rating in the daily living of progressive supranuclear palsy patients (Abstract). Further,

Parkinsonian symptoms (as evaluated by the Unified Parkinson's Disease Rating Scale) were unaffected by donepezil treatment (Table 2).

These articles plainly demonstrate that the art of treating motor function in Parkinson patients is extremely unpredictable, particularly in the case of donepezil being used to treat motor impairments (*i.e.* Parkinsonism).

2. The breadth of the claims

The claim is extremely broad insofar as it discloses the general treatment of "one or more motor dysfunctions caused by Parkinson's disease" with the same compound.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for determining the particular administration regimes (dosages, timing, administration routes, etc.) necessary to treat all symptoms of Parkinson's disease, particularly motor dysfunctions. The working example demonstrates that donepezil is effective in treating dementia in Parkinson patients. However, donepezil treatment had no effect on motor dysfunction (pages 17-18 and Figure 4). In fact, applicant states, "there was no deterioration in parkinsonism in the patients on donepezil" (pages 17-18). Nowhere is it suggested that motor dysfunction was improved or treated by donepezil. Thus, the applicant at best has provided specific direction or guidance only for the treatment of dementia caused by Parkinson's disease. No reasonably specific guidance is provided

concerning useful therapeutic protocols for the treatment of motor dysfunctions caused by Parkinson's disease.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that donepezil could be predictably used as a treatment for motor dysfunctions caused by Parkinson's disease as inferred in the claims and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 21-22, 25-27, 30-32, 35, 37 and 40 are rejected under 35 U.S.C. § 102(a) as being anticipated by Henneberg (J. Neural. Transm., 1999) (prior art of record).

Applicant's arguments have been considered and are persuasive in part. Firstly, applicants argue that Henneberg is not prior art under 35 U.S.C. § 102(b) as it was published in April 1999 and the instant invention has a priority date of March 3, 2000. This argument is

persuasive and the rejection against the instant claims has been changed to a rejection under 35 U.S.C. § 102(a). Secondly, applicant argues that Henneberg has not been "peer reviewed" and has not been statistically analyzed. This argument is not persuasive because there is nothing in the patent law that requires prior art to be peer reviewed, only that it be "published". Henneberg is clearly published prior art. Thirdly, applicant argues that there is no evidence that the patients in Henneberg's study did not suffer from Alzheimer's dementia in a manner "wholly unrelated to Parkinson's disease". This argument is not persuasive. Henneberg's article is titled, "Cognitive dysfunction in Parkinson's disease (**Parkinson-plus dementia**) – successful treatment by Donepezil (Aricept®)". Henneberg explicitly states that the patients "*suffered from* idiopathic or symptomatic **Parkinson's disease and dementia**" and were "treated with Donepezil". Thus, Henneberg is clearly treating patients with Parkinson's disease by administering Aricept®. The rejection is maintained and reiterated below.

The instant claims recite the treatment of "dementia or one or more cognitive impairments caused by Parkinson's disease" by orally administering 5 to 10 mg donepezil.[2]

Henneberg teaches the treatment of patients suffering from idiopathic or symptomatic Parkinson's disease and dementia by administering Aricept®. Aricept® was administered at night in a dose of 2.5 mg and in "most cases" 5 mg/day was applied (XXV, "Patient and methods"). Aricept® is commercially available for oral administration is film-coated tablets containing 5 mg or 10 mg of donepezil hydrochloride (see ARICEPT® U.S. Prescribing Information, previously cited). 44 out of 64 "showed remarkable improvement of their psychopathological state within 14 days" (*id.*, "Results"). Henneberg concludes, "Donepezil has

[2] Donepezil is also known as Aricept®, a registered trademark of Pfizer, Inc.

been shown to be of value in the treatment of "Parkinson-plus (dementia) in 44 of 64 patients" (*id.*, "Discussion and conclusions"). Although Henneberg reports on subjective criteria, the fact remains that donepezil hydrochloride was administered to patients having Parkinson's disease in the doses instantly claimed. Henneberg further states that a study using "objective criteria (Folstein's minimental state examination, reaction times, tests of short term memory) has been started at the Hospital for Parkinson's Disease" (XXVI).

Henneberg thus anticipates the subject matter claimed in instant claims 21-22, 25-27, 30-32, 35, 37 and 40.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 21-35 and 37-40 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Henneberg (J. Neural. Transm., 1999) in view of Sugimoto *et al.* (U.S. Patent No. 4,895,841; Issued January 3, 1990) (prior art of record).

Applicant's arguments have been considered but are not persuasive. Firstly, applicant argues that Sugimoto is "unrelated to the claimed invention". This argument is not persuasive. Sugimoto discloses the instantly claimed compound (*i.e.* donepezil). As such the reference is clearly related to the claimed invention. Secondly, applicant argues that Sugimoto does not disclose or suggest that donepezil could be useful in treating dementia caused by Parkinson's disease. This argument is also not persuasive because Henneberg teaches such treatment, as discussed *supra*. Sugimoto is used to show that enantiomers of donepezil were known in the art,

not to show that donepezil could be used to treat Parkinson's dementia. However, examiner notes that Sugimoto does discuss that the disclosed compounds inhibit acetylcholinesterase and can be used in the treatment of various kinds of dementia. The rejection is maintained for the reasons of record and reiterated below.

Henneberg discloses as applied to claims 21-22, 25-27, 30-32, 35, 37 and 40, *supra*. Claims 23-24, 28-29 and 38-40 differ over Henneberg in requiring a stereoisomer of donepezil. Claims 33-34 recite topical administration of donepezil hydrochloride.

Sugimoto *et al.* disclose that donepezil and its stereoisomers are useful in the methods described therein (see especially col. 12, lines 30-48 and col. 34, Example 4). The patent specifically discloses the cyclic amine compounds of the present claims (cols. 2-12), as well as explicitly describing donepezil (Example 4), its hydrochloride salt (col. 12, line 31 and Example 4), and stereoisomers of the disclosed compounds (col. 12, lines 44-48). They further disclose that the disclosed compounds (*e.g.* donepezil) are capable of inhibiting acetylcholinesterase and are thus effective for the treatment of various kinds of dementia and cerebrovascular diseases (col. 29, lines 52-65). The patentees further disclose effective dosages of from generally 0.1 to 300 mg and specifically 1 to 100 mg per day (col. 30, line 25, compare to, *e.g.*, instant claims 30 and 40). The compounds may be orally administered (col. 30, lines 10-11) and presented in a variety of dosage forms, such as injections, suppositories, sublingual tablets, tablets, and capsules (col. 30, lines 27-31).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

In the instant case, Henneberg clearly teaches that donepezil hydrochloride (*i.e.* Aricept®) is subjectively effective in treating Parkinson's dementia and further teaches that objective studies are being carried out. As such, there is clear motivation to administer donepezil hydrochloride to Parkinson patients having dementia. Sugimoto *et al.* disclose that donepezil and related compounds can be in the form of hydrochloride salts and enantiomers. The patent further discloses that the compounds can be administered in a variety of dosage forms.

In the absence of a showing of unexpected results commensurate in scope with the claims, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made that enantiomers of donepezil would be useful in treating Parkinson's dementia. The motivation to do so is found in Henneberg who discloses that racemic donepezil hydrochloride (*i.e.* Aricept®) is useful in treating such a condition. The skilled artisan would be well aware that the individual enantiomers of a therapeutically effective racemic compound would also be therapeutically effective (sometimes more effective, sometimes less effective). Sugimoto *et al.* also provides the skilled artisan with the means (synthetic methods, administration routes, doses, etc.) to administer enantiomers of donepezil hydrochloride. In addition, the recited forms of administration (oral and topical) are routine and well known in the pharmaceutical art. As such, the skilled artisan would have been imbued with at least a reasonable expectation of success in treating Parkinson's dementia by administering donepezil hydrochloride, its salts and its enantiomers through various routes of administration.

Thus, the methods of instant claims 21-35 and 37-40 would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson, Ph.D.
Patent Examiner
AU 1614

February 14, 2007

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER

2/14/07